# Research/Recherche

## Global seasonality of rotavirus infections*

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*Data from 34 studies of the etiology of childhood diarrhoea were compiled in order to investigate the seasonal patterns of rotavirus gastroenteritis and consider their implications for transmission of the virus. Rotavirus was detected in 11–71% of children with diarrhoea, and the median rate of detection (33%) was independent of the level of economic development or geographical region of the study area, as well as of the method of detection used. While rotavirus infections have been called a winter disease in the temperate zones, we found that their incidence peaked in winter primarily in the Americas and that peaks in the autumn or spring are common in other parts of the world. In the tropics, the seasonality of such infections is less distinct and within 10° latitude (north or south) of the equator, eight of the ten locations exhibited no seasonal trend. Throughout most of the world, rotavirus is present all the year round, which suggests that low-level transmission could maintain the chain of infection. The virus is spread by the faecal–oral route but airborne or droplet transmission has also been postulated. The epidemiology of rotavirus–its seasonality in the cooler months, its universal spread in temperate and tropical zones in developed and less developed settings–more closely resembles that of childhood viruses that are spread by the respiratory route (such as measles) than that of common enteric pathogens that are spread predominately by the faecal–oral route.*

### Introduction

Seasonality is an important but poorly understood feature of rotavirus diarrhoea. "Winter gastroenteritis" and "winter vomiting disease" were recognized illnesses of early childhood before rotavirus was identified and found to be their cause (*1*, *2*). In temperate climates, rotavirus is most frequently detected in the winter and rarely identified in the summer months (*3*). In contrast, in the tropics, it is detected all year round, with seasonal trends that are less well defined (*4*). Attempts to explain these findings have tried to relate disease incidence to climatological factors such as rainfall, humidity, and temperature, but no clear conclusions could be drawn (*5–7*).

Recently, in the course of reviewing the seasonality of rotavirus infections in the USA, we noted that the peak season occurred in the autumn in the south-west and extended into the spring in the north-east of the country (*8*). Moreover, the peaks of rotavirus activity occurred earlier in Central America and Mexico and appeared to traverse the USA from south-west to north-east in a repetitive yearly pattern, which raises questions about the reservoir and the mode of transmission of this infectious agent.

Here, we review data on the seasonality of rotavirus infections from surveillance studies conducted in a large number of countries, describe the global patterns of rotavirus gastroenteritis, consider the implication of these patterns for transmission, and compare the global trends with those for other childhood viral diseases whose mode of transmission has been established.

### Methods

To examine the global trends in the seasonality of rotavirus infections, we reviewed the results of epidemiological studies of childhood diarrhoea from a wide range of countries on the monthly incidence of rotavirus gastroenteritis. The studies were identified from a Medline search of papers published over the period 1974–88, using the following keywords: rotavirus, season, and epidemiology. This list was

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extended by including also references from a recent review of rotavirus epidemiology (*9*). Studies were selected in which children had sought care from a hospital, clinic, or medical practitioner for gastroenteritis and in which the methods used to detect rotavirus were clearly described. Studies were included if they satisfied the following criteria: conducted continuously for 1 year or more; reported more than 50 confirmed cases of rotavirus diarrhoea; and described monthly data on the proportion of all patients with diarrhoea caused by rotavirus.

The proportion of diarrhoeal cases caused by rotavirus was selected as a criterion because its accuracy was not dependent on the use of strict sampling methods, it was reported in most studies, and it could clearly reflect seasonal trends. Because of differences in the background rates of diarrhoea between locations and the range of paediatric age groups included in different studies, we could not compare the absolute numbers of cases between studies. However, comparisons were made of trends within studies. For surveys that covered more than 1 year, the numbers of cases were combined by month to give the proportion of confirmed rotavirus cases per month.

To review the seasonality of rotavirus infections, we plotted and arranged by geographical area and latitude the monthly proportion of diarrhoea cases for the year that were positive for rotavirus. The median proportion of all diarrhoea caused by rotavirus was calculated for each study. Peaks were defined as points above the median for each study so that, in general, 6 months should lie above and 6 months below this value each year. Winter was defined as December–March in the northern hemisphere and June–September in the southern hemisphere.

## Results

A total of 34 studies from 23 countries on six continents between latitudes 60° north and 38° south met all the study criteria and were included in the analysis (Table 1). The studies differed in many aspects of their design, diagnostic methods used, patient characteristics, and duration (range, 1–4.5 years; 15 studies were continued for more than 1 year). The studies were conducted between 1974 and 1987 and included data on surveillance populations that ranged in size from 130 to 1727 children. In some studies, enrolment was strictly limited to children aged less than 2 years; in others, children of all ages were included. However, because of the predilection of diarrhoeal disease for infants and young children, the majority of patients in most studies were under 3 years of age. The definitions of diarrhoea, when stated, were quite similar.

The mean percentage of patients in whom rotavirus was detected was independent of any differences in study design and survey population (Table 2). The rates of detection in studies that used electrophoresis were slightly lower than those in which electron microscopy or immunoassays were used. Otherwise, detection rates were similar in studies with different age criteria, patient populations (hospital versus clinic), or geographical location (tropical versus temperate climate).

We examined first the hypothesis that rotavirus infections are a winter phenomenon in temperate zones (Fig. 1). In the Americas, six of seven temperate cities examined had distinct winter peaks. For all other temperate locations there was a clear seasonal peak, but in only 3 of 11 studies did it occur in the winter; in 5 the predominate rotavirus season occurred in the autumn; and in 2 in the spring. The only exception to this trend was in Pôrto Alegre, where an unusual and distinct peak occurred in summer (*20*).

In the tropics (between latitudes 23°27′ north and south of the equator), the seasonality was less distinct. Of 10 surveys conducted within 10° latitude north or south of the equator, 8 exhibited no distinct seasonal trend. Farther from the equator, at latitudes 10° to 23°27′ north or south, five of six studies showed a distinct seasonal peak—two in winter, two in the autumn and winter, and one in the autumn.

Throughout most of the world, rotavirus is present all the year round and the infections it causes are diagnosed every month of the year. In only 5 of the 33 cities—Osaka, Bangkok, Winnipeg, Ann Arbor, and Washington, DC—was rotavirus not detected for two consecutive months in patients with diarrhoea.

Data from the 15 studies that continued for longer than 1 year were reviewed in order to test the stability of the seasonal peaks shown in Fig. 1. In no study did the peak differ by more than 1 month from those shown.

## Discussion

One of the most prominent epidemiological features of rotavirus gastroenteritis is commonly held to be its winter seasonality. This feature of the disease was recognized even before the virus was discovered and was confirmed by early studies. The results of our review suggest the hypothesis that in temperate climates the winter seasonality of rotavirus infections is too simple a generalization; globally, rotavirus is certainly more common in the cooler months, but the seasonal peaks of the infections can vary broadly and

Table 1: **Summary of the results of the 34 studies of rotavirus infections that were reviewed in the study**

| City | Reference | Study period | Patients | | Age group (years) |
|---|---|---|---|---|---|
| | | | Number[a] | % with rotavirus[b] | |
| *North America* | | | | | |
| Winnipeg | *10* | 1974–75 | 472 | 11 (E) | <16 |
| Toronto | *11* | 1975–76 | 1541 | 20 (E) | Paediatric[c] |
| Ann Arbor | *12* | 1978–80 | 199 | 35 (I) | Paediatric |
| Washington, DC | *13* | 1974–78 | 604 | 39 (E, I) | ≤4 |
| Houston | *14* | 1985–87 | 380[d] | 25 (I) | <3 |
| Mexico City | *15* | 1977–78 | 242 | 25 (E, P) | <5 |
| San Jose | *16* | 1976–77 | 130[d] | 38 (E) | <3 |
| *South America* | | | | | |
| Caracas | *17* | 1975–76 | 293[d] | 41 (E) | <5 |
| Belem | *18* | 1980 | 187 | 42 (E, P) | <6 |
| Guayaquil | *19* | 1978–81 | 1722 | 22 (E) | <6 |
| Pôrto Alegre | *20* | 1981–82 | 388 | 42 (E, I) | <5 |
| Santiago | *21* | 1979–81 | 615[e] | 22 (P) | Paediatric |
| *Europe* | | | | | |
| Tampere | *22* | 1977–78 | 159 | 60 (I) | <15 |
| Uppsala | *23* | 1981 | 416[e] | 45 (E) | <15 |
| Birmingham | *24* | 1974 | 258[d] | 38 (E) | <6 |
| London | *25* | 1977 | 152 | 51 (E) | <13 |
| *Africa* | | | | | |
| Addis Ababa | *26* | 1977–78 | 962[d] | 28 (P) | Paediatric |
| Bangui | *27* | 1981–82 | 1197[e] | 18 (I) | <15 |
| Nairobi | *28* | 1981–83 | 386 | 39 (I) | <2 |
| Nairobi | *29* | 1975–76 | 160 | 41 (E) | Paediatric |
| Pretoria | *30* | 1983–85 | 788 | 23 (I) | <2 |
| *Asia* | | | | | |
| Lanzhou | *31* | 1982–85 | 882 | 38 (E) | <2 |
| Osaka | *32* | 1980–82 | 395[d] | 31 (E) | <10 |
| Shanghai | — | 1981–85 | 632[d] | 28 (P) | Paediatric |
| New Delhi[f] | — | 1985 | 330 | 15 (I) | <5 |
| Calcutta | *34* | 1979–81 | 245 | 22 (I) | <12 |
| Hong Kong | *35* | 1983–84 | 899 | 28 (I) | <5 |
| Bangkok | *36* | 1977–80 | 179 | 31 (E) | <3 |
| Calicut | *37* | 1976–78 | 368 | 71 (E) | <5 |
| Vellore | *38* | 1983–85 | 916 | 18 (E,I) | <3 |
| Kuala Lumpur | *39* | 1982 | 810 | 40 (I) | <5 |
| Yogyakarta | *40* | 1978–79 | 334 | 38 (E) | <12 |
| *Oceania* | | | | | |
| Perth | *41* | 1980–81 | 975[e] | 13 (I) | Paediatric |
| Melbourne | *42* | 1975–76 | 400 | 42 (E,P) | Paediatric |

[a] Hospitalized patients unless otherwise noted.
[b] Letters in parentheses indicate the detection method used. P = polyacrylamide gel electrophoresis and countercurrent immunoelectrophoresis; I = enzyme-linked immunosorbent assay and radioimmunoassay; and E = electronmicroscopy and immuno-electron-microscopy.
[c] Paediatric = age group not specified.
[d] Clinic patients only.
[e] Clinic and hospitalized patients combined.
[f] **Jayashree, S.** *Passive immunity to rotavirus infection during early infancy.* Ph.D. thesis. All India Institute for Medical Sciences, New Delhi, 1988. See also: **Bhan, M.K. et al.** Role of enteric adenoviruses and rotaviruses in mild and severe acute diarrhoea. *Pediatric infectious diseases journal*, **7**: 320–323 (1988).

occur from autumn to spring. Strict winter seasonality was common only in the Americas and was the exception in other parts of the world. The range of the timing of the rotavirus peaks indicates that temperature alone does not account directly for this broad seasonal pattern. Other factors related to host behaviour, and the spread and survivability of the virus must also be involved.

Studies in the USA have repeatedly found periods of two or more consecutive months when rotavirus was not detected. In view of the small sample sizes in these studies, however, it is not clear

whether rotavirus was truly absent, or more likely, whether it was present at a level that was lower than the limit of detection. If rotavirus were truly absent at certain periods, its reappearance at the beginning of the next season would require either the introduction of a new strain from outside or the re-emergence of old strains from some as yet unidentified reservoir in the environment. Laboratory studies to characterize strains from the beginning of the rotavirus season could help to determine the source of the virus and to distinguish between these two possibilities. The global pattern presented by rotavirus infections is quite distinct. In most of the world, the virus is present throughout the year, which suggests that low-level transmission occurs all the year round and that humans are a suitable reservoir.

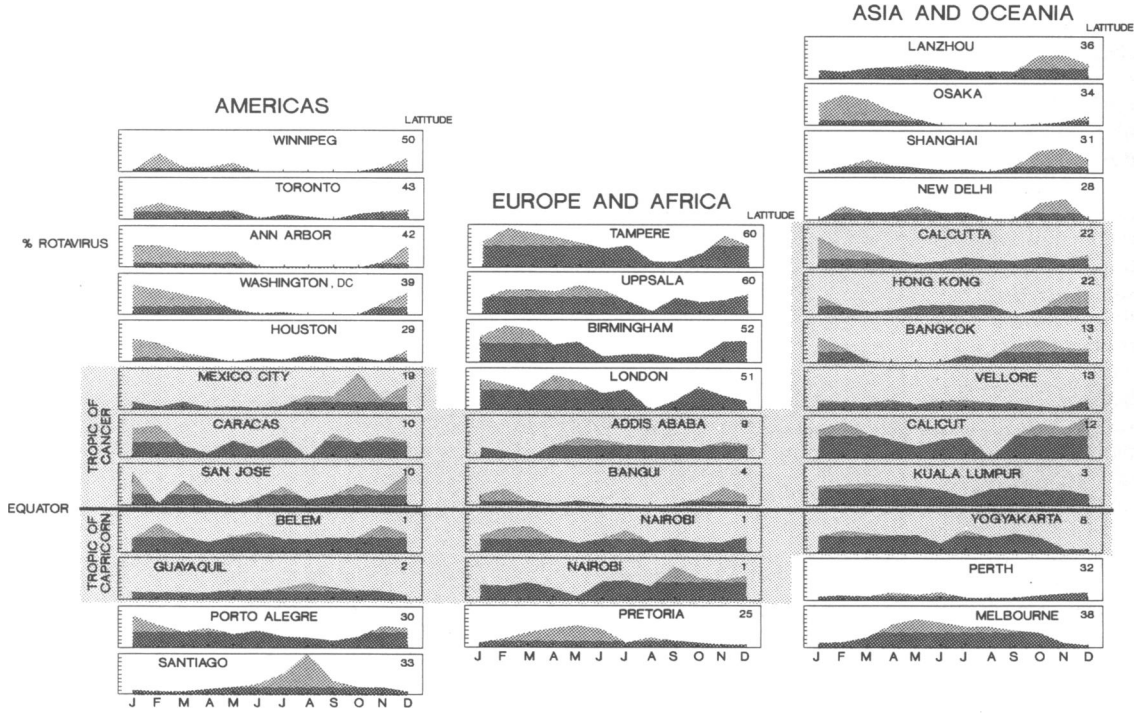
Comparison of the seasonality of rotavirus infections with that of other illnesses of childhood provides some insights into the possible modes of transmission: faecal–oral and airborne droplet. The faecal–oral route has been established in various

Table 2: **Summary of the results of rotavirus detection among children with diarrhoea in the 34 studies, by four design variables**

| Design variable | No. of studies | % children with rotavirus (mean ±SD) |
|---|---|---|
| *Method of detection* | | |
| Electron microscopy | 14 | 36.9±14.5 (11–71)[a] |
| Immunoassay | 11 | 28.9±13.8 (13–60) |
| Electrophoresis | 3 | 26.0± 3.5 (22–28) |
| *Age limit* | | |
| ⩽3 years | 7 | 30.3± 8.4 (18–39) |
| ⩽6 years | 12 | 36.2±14.1 (15–71) |
| All others | 15 | 31.6±14.4 (11–60) |
| *Patient source* | | |
| Hospital | 23 | 34.5±14.4 (11–71) |
| Clinic | 7 | 32.7± 6.2 (25–41) |
| Hospital and clinic | 4 | 24.5±14.1 (13–45) |
| *Latitude category* | | |
| Temperate | 18 | 32.2±13.6 (11–60) |
| Tropical | 16 | 33.9±13.1 (18–71) |

[a] Figures in parentheses are the range in percent.

Fig. 1. **Monthly rate of occurrence of rotavirus among children with diarrhoea in 34 selected studies whose locations are arranged according to latitude. The ordinates show the percentage (0–100%) of total diarrhoea cases each month associated with rotavirus. Lightly shaded areas indicate peaks above the yearly median. The bold line identifies the equator, and the shaded boxes show the cities within the tropics. The approximate latitude of each city is noted in the upper right-hand corner of each chart.**



geographical settings (*43, 44*), for travellers with diarrhoea (*45*), and in volunteer challenge studies (*46, 47*); it has not been proven, however, for the transmission of endemic childhood rotavirus diseases. Airborne-droplet spread has been suggested because rotavirus infections are universal diseases of children during their first 4 years of life, regardless of the level of hygiene that prevails or of the quality of food and water. Children in developed countries are infected at the same ages and as frequently as those in less developed countries. Moreover, epidemic diarrhoea in infant mice (EDIM) is transmitted by airborne droplets (*48*), and in some studies, rotavirus infection has been associated with respiratory symptoms in humans (*25, 49*).

The epidemiology of rotavirus shows some striking similarities to that of measles in the prevaccine era—a disease believed to be transmitted by infectious droplets (*33, 50–53*). First, measles is a "well-behaved" disease with a consistent seasonal pattern and major peaks in winter. Second, in temperate climates, measles is a disease of the cooler months, often associated with school terms. Third, measles infections are nearly ubiquitous, and affect most children in developed and developing countries by the time they have reached 5 years of age. Finally, measles can occur explosively, infecting $>80\%$ of susceptibles as it passes. The biennial peak that exists for measles has not yet been demonstrated for rotavirus. These features in the epidemiology of rotavirus clearly distinguish it from the routine bacterial pathogens that cause diarrhoea whose faecal–oral mode of transmission is focal, where infection is not ubiquitous, and where disease activity often occurs during summer.

Several limitations must be underscored in the analysis of the data. Perhaps the most important is the lack of data from more than 1 year with which to test the consistency of seasonal trends. Analysis of such data that were available nevertheless indicated that there was little variation in the peak season for rotavirus infections in temperate zones but greater variation in the tropics. Limitations that arose because of differences in the methods used to detect rotavirus, in clinical settings, and in the ages of patients were apparently unrelated to the variations in the overall detection rates of the virus. Since our aim was to compare seasonal trends rather than the incidence of disease, considerable variation was acceptable. The small number of studies that met our selection criteria have indicated global patterns for rotavirus infections. The availability of a broader, more representative sample of geographical locations would, however, be useful in carrying out further studies to confirm our observations.

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## Résumé

### Variations saisonnières des infections à rotavirus dans le monde

Le caractère saisonnier des gastro-entérites à rotavirus est un phénomène bien connu mais encore mal compris. Dans le présent article, on s'est intéressé à l'aspect saisonnier des infections à rotavirus dans le monde en passant en revue les études épidémiologiques sur la diarrhée infantile. Les informations sur la survenue mois par mois de la diarrhée à rotavirus chez l'enfant ont été tirées d'études ayant été menées pendant au moins un an, comportant au minimum 50 cas confirmés, et qui fournissaient des données mensuelles sur le pourcentage de malades atteints de diarrhée à rotavirus. On a choisi 34 études couvrant des villes de 22 pays et des endroits situés entre 60° de latitude nord et 38° de latitude sud.

La première hypothèse examinée était que les infections à rotavirus surviennent surtout en hiver. Dans les Amériques, six des sept villes étudiées montraient des pics très nets pour ces infections en hiver. Dans toutes les autres zones tempérées, on a observé des pics saisonniers très nets, mais ils ne se produisaient en hiver que dans 3 études sur 11; 7 montraient des pics printaniers ou automnaux, et dans une étude—effectuée à Porto Alegre, Brésil—le pic s'était produit en été. Sous les tropiques, l'aspect saisonnier de ces infections est moins marqué. Sur les 10 endroits situés à moins de 10° de latitude (nord ou sud) de l'équateur, huit ne montraient aucune tendance saisonnière. Dans les endroits plus éloignés de l'équateur, cinq études (sur 6) ont montré des pics nets en hiver, en automne ou au printemps. Comme le pic hivernal n'a été rencontré couramment que dans les Amériques tempérées, la température seule ne peut expliquer les variations saisonnières observées. Les rotavirus sont présents tout au long de l'année dans la plupart des pays du monde, ce qui laisse à penser qu'une faible transmission a lieu toute l'année à partir d'un réservoir endémique.

On a montré que les rotavirus étaient transmis

par voie fécale-orale dans des études chez des volontaires, lors de certaines épidémies et chez les voyageurs. Toutefois, le mode de transmission n'a pas été établi dans la plupart des cas enregistrés chez l'enfant. On a également émis l'hypothèse que ces germes étaient répandus par voie aérienne et par les gouttelettes de Flügge. L'épidémiologie des infections à rotavirus avec son pic saisonnier dans les mois les plus frais, et son extension générale dans les zones tempérées et tropicales, développées ou non, fait davantage penser aux maladies virales infantiles transmises par voie respiratoire (comme la rougeole) qu'à celles surtout transmises par voie fécale-orale (comme la poliomyélite).

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